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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,869	02/11/2005	Kathleen Clarence-Smith	05933.0016.PCUS00	3009

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EXAMINER	
HOUGHTLING, RICHARD A	
ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
03/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,869	CLARENCE-SMITH ET AL.	
	Examiner	Art Unit	
	Richard A. Houghtling, Ph.D.	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6 and 8-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *6 and 8-16* is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Examiner acknowledges receipt of Applicant's response to the restriction requirement filed on October 4, 2007. Applicant elected Group III, claims 8-11 drawn to a R(+)-2-amino-3-hydroxypropanoic acid derivative of Formula (III) with traverse. Applicant's arguments, see Response to Election/Restriction, "The Remarks", filed 01 November 2007, with respect to the compound claim 12 should be included in Group III and be examined with claims 8-11 have been fully considered and are persuasive. Claim 12 is now included in Group III and will be examined on the merits herein.

Applicant further elected a species R(+)-N-[(4,4-diphenyl)-3-butenyl]-2-amino-3-hydroxypropanoate, with traverse. Applicant traversed on the grounds that the compounds defined by the Markush groups of R' and R" are closely related, sufficiently few in number and share a common utility of treating cognitive disorders that a search may be made without serious burden.

Examiner has fully considered Applicant's remarks and they are not found persuasive. Furthermore, the claims encompass methods using hundreds of different compounds, which are contained in many different compositions. The compounds vary distinctly in their structures and functions. Thus, an individual search is required of each individual compound.

Status of the Claims

2. Claims 1-16 are pending; claims 5 and 7 were cancelled in the amendment filed on 01 November 2007 and claims 14-16 were added. Claims 8-12 and 14-16 read upon the elected subject matter and are examined on their merits, herein.

3. Claims 10-12 and 15-16 are directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(B), claims 1-4 and 6, directed to the process of making or using an allowable product, previously withdrawn from consideration as a result of a restriction requirement, are hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Because all claims previously withdrawn from consideration under 37 CFR 1.142 have been rejoined, **the restriction requirement as set forth in the Office action mailed on 04 October 2007 is hereby withdrawn**. In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 3-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating schizophrenia, does not reasonably provide enablement for treating autism, Alzheimer's disease or the entire genus of CNS disease which is accompanied with cognitive disorders or mnestic disorders. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Comment [S1]: Please use form paragraph 7-31-02 for scope of enablement...I think schizophrenia is enabled.

The instant claims 1 and 3-4 are drawn to a method for the treatment of CNS diseases which are accompanied with cognitive disorders or mnestic disorders. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands,* 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman,* 230 USPQ 546 (BdAPIs 1986) at 547 the court recited eight factors:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Nature of the invention: The instant invention pertains to methods and pharmaceutical compositions for treatment of patients suffering from CNS diseases which are accompanied with cognitive disorders or mnestic disorders.

Breadth of the claims: The instant claims embrace treating patients suffering from the entire genus of CNS diseases which are accompanied with cognitive disorders or mnestic disorders to specific CNS diseases including: schizophrenia, autism and Alzheimer's disease.

State of the art: The skilled artisan would view that treatment of patients suffering from any CNS disease associated with cognitive disorders or mnestic disorders, autism or Alzheimer's using glycinergic agonists to be not well established in the prior art. The examiner is unaware of any nexus between the glycinergic neuropathway and the herein claimed diseases states. Furthermore, it is not known in the art to employ compounds affecting the glycinergic neuropathway for treating all CNS diseases accompanied by cognitive disorders or mnestic disorders or the specific CNS diseases claimed, such as, autism or Alzheimer's disease. In contrast, schizophrenia is known in the prior art to be treated using compounds which affect the glycinergic neuropathway.

Relative skill of those in the art: The relative skill of those in the art is high, typically requiring an advanced professional degree.

Predictability or lack thereof in the art: The skilled artisan would view that treatment of CNS diseases which are accompanied by cognitive or mnestic disorders, such as autism or Alzheimer's disease to be highly unpredictable; whereas treatment of

schizophrenia using glycine agonists to be more predictable. Applicant's specification discloses teachings in the prior art which demonstrate that D-serine is a very good agonist of the NMDA glycine receptor but that it has a lower affinity. Further the specification teaches that cognitive symptoms of schizophrenia can be treated with glycine, glycinamide, threonine and D-serine (see p. 1, lines 25-31) and that a clinical trial demonstrated that administration of a dose of D-serine (2 g/day) is an effective treatment of schizophrenia patients reticent to conventional therapies.

The specification does not disclose any teachings from the prior art which demonstrate that D-serine acting as an agonist of the NMDA glycine receptor is known in the prior art to have any beneficial effects in patients suffering from either the claimed CNS diseases autism (claim 3) or Alzheimer's disease (claim 4) or any other CNS disease which is accompanied with cognitive disorders or mnestic disorders, such as for example, Down's syndrome. In lieu of teachings from the prior art that establish the predictability of treating other CNS diseases accompanied with cognitive or mnestic disorders, such as those found in Down's syndrome, Alzheimer's disease or autism; a skilled artisan would require specific teachings from Applicant that demonstrate how to use the invention commensurate with the scope of the instant claims.

In the instant case, Applicant teaches how to make the chemical compounds of the invention, but fails to disclose any teachings or evidence to support beneficial effects of the claimed invention for treatment of cognitive disorders or mnestic disorders found in patients or animal models of any CNS diseases. In lieu of established utility in the prior art or teachings by Applicant, a skilled artisan would render the claimed

treatments as highly unpredictable. Furthermore, to practice Applicant's invention as instantly claimed without any teachings from the prior art or evidence of working examples, a skilled artisan would be faced with the burden of undue experimentation in order to practice the methods for treating all CNS diseases which are accompanied by cognitive or mnestic disorders. Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP §2164.

Genetech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague limitations of general ideas that may or may not be workable.

Therefore, in view of the ***Wands*** factors, e.g., the amount of direction or guidance provided, absence of working examples, and the predictability of the art discussed above, to practice the claimed invention herein, a skilled artisan would have to engage in undue experimentation to test each of the claimed compounds for each and every CNS disease associated with cognitive disorders or mnestic disorders, including those associated with autism or Alzheimer's disease as found in the instant claims as to whether administration of Applicant's claimed compounds do in fact improve cognitive or mnestic disorders associated with CNS diseases and must do so with no assurance of success.

Comment [S2]: Also please address the breadth of the claim,...can be a one or two-liner saying the claims are so broad that encompass any cognitive disorder...or something like that. Also address the level of one skill of the art.

Claim Objections

5. Claim 2 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard A. Houghtling whose telephone number is (571) 272-9334. The examiner may normally be reached Mon-Thurs 8:30 am - 5:00 pm and alternate Fridays 8:30 am - 12:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan may be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RAH

Patent Examiner

/San-ming Hui/

Primary Examiner, Art Unit 1617